

VICTOR J. DZAU:

OK, so we are very excited about this year's annual meeting and today's program, the theme, Women's Health: From Cells to Society. As you see, it will feature a fantastic lineup of speakers who discuss important critical issues on women's health. It ranges from basic research to population and to public health and policy. So this meeting turns out prompts you very exciting. I do want to first thank our program committee members. They include NAM counselors Karen DeSalvo who is the chair of this whole program. Jose Escarce, Mae Jemison, Christine Seidman, and Huda Zoghbi. And then, of course, we have expert participation of Jocelyn Frye, Iffath Hoskins, JoAnn Manson, Herbert Peterson and most importantly, the great, great work of Jessica Marks, our staff. (APPLAUSE). So I'll say this again, can you help me thank the organizing committee and the work of my staff. So on the website, you find today's program speakers, bios, disclosure statements, information about planning committee, and other relevant background and I encourage you to take a look.

In addition, if you are being live tweeted the meetings being live tweeted on using the #NAMMTG spelled M-T-G as meeting. You can see on the screen here. Oh, it's not up there yet, but I'd like to invite therefore at this time to the podium, the chair of the planning committee, Karen DeSalvo who introduced the program, keynote speaker. As you all know, Karen is the chief health officer of Google and a member of the NAM Council. We're so glad that she is, in fact, playing all these roles. Previously, she served as acting assistant Secretary of Health, National Coordinator for Health Information Technology and the director of the Office of National Coordination for Health Information Technology at HHS. Please join me in welcoming Karen DeSalvo.

KAREN DESALVO:

Thank you so much, Victor, and welcome everybody to our 53rd Annual meeting for the National Academy of Medicine. I think we have a really great program lined up for today, and I'm looking forward to all the learnings that are here to come. I do wanna take a minute to echo Victor, and recognize that today is Indigenous Peoples Day, and take a moment to honor elders past, present, and future. The program came together through the diligent work of the program Committee which victors shared the names for. And I hope you'll look in the program and when you see them, thank them in the hallways. It couldn't be done without their valuable contributions. And importantly, I'm also really grateful to the staff for their intellectual input, but also for all the work they do to make sure the logistics work for us so that we can enjoy the meeting. And I do certainly wanna thank all of our speakers and the moderators. I think we have a really interesting, thoughtful and thought-provoking meeting today that's gonna help guide us to action.

Our program today will cover women's health from cells to society. We'll talk about the challenges in women's health because they have never been greater than they are today. And not only will we discuss these challenges, but we will also talk about solutions. Biologic, environmental, behavioral, and cultural factors contribute to sex and gender disparities with respect to disease, disease progression, health care access, and outcomes. Women also have different lived experiences. They are more often facing health care gaslighting during medical appointments, and are more likely to work in low wage jobs and more likely to be employed less than full time. They're also at higher risk of personal violence. All these challenges are particularly true for women of color and marginalized communities. Women have unique health needs across their lifespan, and their health outcomes often differ from men. These needs have been historically underrepresented in research, clinical care, and policy or programmatic initiatives.

No doubt women's maternal and reproductive health represents an area of immediate need and pressing concern. Women in the US have the highest rate of maternal deaths compared to all other high income countries, and there are large sociodemographic, geographic and racial and ethnic disparities. For example, indigenous women are three to three times more likely to die from pregnancy related causes than non-Hispanic white women. The US Supreme Court's ruling to overturn Roe V Wade has brought reproductive health care further to the forefront of national attention, and is making it more difficult for women to access safe, high quality care. The risks are especially acute for women of color, from low income backgrounds and those living in rural areas. While reproductive health is perhaps the most discussed aspect of women's health today, women's health is about more than reproductive health. They live most of their lives outside of the reproductive life stage. And across their lifespan, they face disproportionate risk for a variety of health conditions.

In research, female animal models are still frequently excluded from basic research. Women, particularly women of color are often underrepresented in clinical trials, and pregnant and lactating people are often excluded from clinical research. Today, our program will examine these issues across the lifespan, from cells to society, and identify challenges and gaps but we will also identify steps to improve women's health outcomes. The scientific program will feature three panels. The first is on sex and gender differences, the next on maternal and reproductive health. And finally, we will move to healthy longevity for women. The program will conclude with the Presidents Forum, moderated by Dr Zhao, and which will center on accelerating progress and exploring future directions in policy and research on women's health. OK, so now for some general logistical information following the panelists remarks and the moderated Q&A, we'll have about 20 minutes for audience questions. For those of you who are here in person, we have microphones in the aisles, you can line up at those mics.

If you're unable to access the mic, just raise your hand in one of the NAM staff will come and help you. We'll also be taking questions from the audience online. So the virtual audience wants to use the Q&A tool in the live stream, the NAM staff will be moderating that.

KAREN:

And now it is my great honor to introduce our keynote speaker, Dr Paula Johnson. Dr Johnson is a pioneer who brings decades of experience in the fields of academic medicine, public health, and education. Since becoming the president of Wellesley in 2016, she has placed the college at the forefront of STEM education for women and has led the creation of the school's new strategic plan, which places inclusive excellence at the heart of the Wellesley experience. President Johnson has held several leadership roles in her career as a physician-scientist. She most recently served as the Grace A Young Family Professor of Medicine in Women's Health at Harvard Medical School and professor of epidemiology at Harvard TH Chan School of Public Health. She founded the Connors Center for Women's Health and Gender Biology at Brigham and Women's Hospital. She's a member of the National Academy of Medicine and the American Academy of Arts and Sciences. She's received several honorary degrees and numerous awards for her contributions to science, medicine, and public health.

And I must say, I've had the opportunity to have a few conversations with Dr Johnson in preparing for this meeting, and she embodies grace, strength, leadership, and is a truly inspiring person. And I'm very much looking forward to your remarks today. Please join me in welcoming Dr Johnson. (AUDIENCE APPLAUSE)

DR PAULA JOHNSON:

Thank you, Karen. Thank you so much. And I wanna thank you and Victor and the committee for giving me this opportunity to address this phenomenal group. And I'm so happy to be kicking off this symposium devoted to women's health. So, today, I wanna cover some history this morning to remind us all of the power that this body has to advocate for an evidence-based approach to women's health, and to set the stage for today's panels by considering an agenda for women's health for the future. Since the predecessor of the National Academy of Medicine - the Institute of Medicine was founded in 1970, The country has looked to us to shape the way that science is done, the way that care is delivered, and the ways that policies can support the well-being of women. For example, we are all wrestling with the impact of the Dobbs decision and its negative impacts on women's health. It's worth remembering that in 1975, as a relatively new organization, the Institute of Medicine conducted a study of legalized abortion as an issue of rights, not as an issue of rights or ethics, but as a public health issue, and found that legal abortion reduced the risk of maternal death compared with illegal abortion and full-term pregnancy.

Alongside its stellar work over the years on maternal and reproductive health, this body has helped to shine a light on the neglect of women's overall health in both scientific research and clinical practice. After thalidomide and other drugs prescribed to pregnant women turned out to cause birth defects, the FDA not only banned pregnant women from being included in clinical trials, it banned all women capable of becoming pregnant. Women were routinely excluded from most medical research. The operative assumption was that what was true for men was generally true for women, and diseases that were more prevalent in women were just basically less studied. Women might not have been making much progress on the healthcare front, but we were making progress in national politics. A key voice in speaking out against this injustice was somebody we recently lost, US representative Pat Schroeder, who served in Congress for 24 years. She said, "It was the famous 1980s physician health study, which found that taking aspirin daily would prevent heart attacks." That tipped her off to the problem.

Every single one of the 22,000 physicians included in the clinical trial was a man, and yet the findings were presented as if they held true for women, too, which we now know is definitely not the case. In 1990, the Congressional Caucus for Women's Issues asked the Government Accountability Office to look at the exclusion of women from medical research funded by the NIH. The GAO found that the NIH was violating its own policies, and in response, the NIH established the Office for Research on Women's Health. By 1993, in both parties in the House and the Senate, led by Pat Schroeder, Olympia Snowe, and Barbara Mikulski - Oh, the days of bipartisanship - ensured that the NIH Revitalization Act included a mandate that women and minorities be included in clinical research. In 1994, the IOM released a report considering the ethical and legal implications of women's exclusion from clinical research. It blisteringly described a medical and scientific culture rife with bias that left women's health unjustly understudied.

The report notably put its finger on the deadly male norm in medical research. The conclusion was that these biases produce findings that are not valid for large segments of the population. Then, in 2001, the IOM released the landmark report exploring the biological contributions to human health, "Does Sex Matter?" It coined the phrase "every cell has a sex". Now, the implications... (AUDIENCE LAUGHS). I know. The implications of that five-word sentence... It's not every cell has sex. Every cell has a sex. The implications of that five-word sentence are vast and all-encompassing, and this body helped the scientific and medical community understand that. Because women and men are different at the cellular and molecular levels - thanks to that 23rd pair of chromosomes, it's not just women's sex organs that

develop differently, but their hearts, their lungs, their immune systems, and more. The intersection of these fundamental genetic differences with the hormonal and reproductive changes across a woman's lifespan have ripple effects on every aspect of her health.

Pharmaceuticals can act differently in men and women. Diseases have different prevalences in women and men and can manifest themselves differently. The report recommended that the investigators consider sex as a biological variable in all biomedical and health-related research, a policy that the NIH would put in place 15 years later. That said, social factors also have a profound influence on the health of women and deserves study. These include gender, race, and other factors. In 2010, with a report titled 'Women's Health Research Progress, Pitfalls and Promises', this body pointed out that the groups of women generally at highest risk of having or dying from a condition, those of lower socioeconomic status, and members of racial and ethnic minorities are the least represented in biomedical research. It takes sufficient data to inform the understanding of vulnerable populations. In addition to its crucial work in illuminating the scientific, clinical, and public health issues surrounding women's health, this body has had an important influence on health policy, helping to make sure that it's evidence-based.

It was truly an honor to have served with several colleagues here today on the Institute of Medicine Committee that in 2011 recommended which preventative services for women should be included in the Affordable Care Act at no cost. For example, we argued successfully that contraception was a preventative service that should be covered without out-of-pocket costs, a critically important evidence-based conclusion after years in which some insurers paid for Viagra prescriptions but not for family planning. In 2014, my research group at the Connors Center for Women's Health at Brigham and Women's Hospital partnered with the Kaiser Family Foundation and the Jacobs Institute for Women's Health on an evidence-based policy report to identify the remaining gaps in scientific research pertaining to sex. 21 years after the 1993 Revitalization Act, the NIH was still not fully living up to its inclusion policies. Among the list of problems we flagged, two stand out. First, there was some progress in the number of women included in trials.

However, even when women were included, the vast majority of federally funded studies still did not report sex-specific findings. Given the biological importance of sex, when you give an average as a result, that is not good for women or men. The second problem we flagged was that in basic and preclinical research, the vast majority of studies continued to be focused on male animals and male cells without sex as a variable. What you have is very poor science. So, here's how Pat Schroeder described the lagging NIH. It reminds me of when you ask your children to move the clothes from the washer to the dryer, then you go back and the clothes are still wet, and they say, well, you didn't tell me to turn the dryer on. So, we're turning on the dryer. In 2016, the NIH finally began expecting that sex be a biological variable factored into the design, collection, analysis, and reporting of all studies it supports. Even asking the question what does sex mean for this study is leading us in important new directions.

Today, we're still wrestling with the issues of representation in research as the Academy's 2022 report 'Improving Representation and Clinical Trials and Research' confirms. That said, we've clearly made some progress. The percentage of participants in NIH-funded trials who are women has increased from 44% in 2013 to 52% in 2018. Our understanding of the different course diseases take in women has improved, but there's so much more to do in research, including understanding why early onset cancers are rising in women and why there's a mental health crisis amongst our youth, with teen girls being impacted disproportionately and more. And there's so much more to do in terms of translating knowledge we gain

through research into clinical care. Maternal mortality is getting worse, not better. Although cardiovascular disease is the leading cause of death for women. Women presenting with chest pain in an emergency room - and I want to say that is the typical symptom - still wait longer to be seen than men and women of color wait the longest.

And we still don't understand the underlying sex differences in the biology of what we see. Women in North America are more likely to have two or more chronic conditions than in other high-income countries. The goal of ensuring that women have equal access to the best evidence-based understanding and treatment remains unrealized. And on the policy front, we seem to be going backwards. In the wake of the Dobbs decision, which reversed decades of progress on women's reproductive health and which is creating healthcare deserts for women around the country, it's time for a bold new agenda for women's health. The National Academy of Medicine has the capacity to have significant influence at this critical moment in time. So, today, I wanna suggest three pillars for any agenda we develop. The first, we must do the fundamental science right and admit how much we still don't know. Second, the title of this meeting, 'From Cells to Society', should represent the approach to the greatest problems in women's health with an effort to understand the biology from the molecule up, and then to translate research into clinical care and public health interventions.

And third, we need health policies and leadership that support the larger goal of gender equity in our society. So, there's a reason why science comes first on my list. It informs every aspect of our healthcare system, from individual patient care to federal policy. When the research is inadequate or misleading, it distorts decision-making throughout the system. Applied mathematician Arthur Miron has shown that when you consider the burden of that disease represents, diseases that are male-dominant are largely overfunded by the NIH, and those that are female-dominant are largely underfunded. But the funding doesn't have the full desired impact if we don't design our studies properly. We're still wrestling with a medical and scientific culture where ignorance about the importance of sex remains rampant. A survey of NIH study section members in 2016 and 2017, after the sex as a biological variable policy was put in place, found that about a third did not believe it was important for all NIH research to consider sex in experimental design.

Another survey conducted in 2020 of scientists who conduct biomedical research using vertebrate animals - and remember, this is four years after the policy was put into place - found that only about half always analyze their findings by sex. Even at the very frontiers of medical research, sex is not always considered. Last year, Dr Sarah Mitchell of Princeton's Ludwig Institute for Cancer Research surveyed the preclinical data for her subspecialty 'anti-aging interventions' focusing on mouse studies of calorie restriction, one of the most investigated interventions. She found that in 2022, a majority of papers didn't consider both sexes, and a minority didn't report sex at all. This hardly makes sense when the important sex differences have been observed. Research by Dr Mitchell has shown that in one strain of mice, both sexes live longer when their calories are restricted by 20%, and that's in the blue lines. But when they're fed 40% fewer calories in the red, the males live longer, but the females die sooner.

Now, that compares with a different experience in another strain where there were no observed sex differences. Now, as a general rule, women outlive men despite generally experiencing worse health, and the diseases of aging have different prevalences in men and women. So, as geroscience, or the study of aging across the lifespan takes off, and we search for geroprotectors to extend both the lifespan and the health span, we need to ensure that differences in the ways women age and respond to

interventions receive the attention that they deserve. We also clearly need to make better use of the sex-based health data that we've accumulated over decades, and to employ the powerful new tools of data science, machine learning, and artificial intelligence to help us find correlations that we might have missed. Within women's health, we also need the equivalent of the revolution that has taken place in the field of cancer in recent years - thanks to advances in molecular biology, genomics and immunology.

We need to replace our rudimentary disease-by-disease model with a focus on the underlying mechanisms of health and disease, which are essential for us to understand the best strategies for prevention and treatment. This also argues for taking a life course approach to women's health to understand how exposures during fetal development and in girlhood affect outcomes during the reproductive years, and then menopause and aging. To do good science, we have to admit how much we don't know, and we must be vigilant in making the most out of every dollar spent on research by considering sex and other critical determinants of health. So, while we commit to good science and to continue to explore the biological impact of sex, it's also clear that social and environmental factors have important influence on health and well-being, including race, ethnicity and gender. So, let's not allow what happened to women happen to other gender minorities in terms of being left out of the research. We need to expand the study of gender to include gender minorities, and to develop strategies to study the health of transgender people across the lifespan, including the impact of hormonal therapy started at different stages in the life cycle.

We must learn how to include the transgender population in clinical trials now. As we consider the etiology of disease, we need to look hard at the rampant inequities at the intersection of race, ethnicity and sex. While research is crucial to making healthcare more equitable, there is no guarantee that it will have an impact. That depends entirely on what we do with it, which brings me to my second point. We need to take a 'Cells to Society' approach to the greatest challenges in women's health. Now, you've already heard maternal and infant mortality offers really a scorching example of why we need an all-in effort. The United States has the dubious distinction of having one of the highest mortality rates, or the highest mortality rate amongst high-income countries, largely because black women fare so poorly. And these gaps persist at every level of education and income. In black women, the number one cause of maternal mortality is cardiac and coronary conditions followed by cardiomyopathy.

Research into reproductive health and cardiovascular health has told us that discrete conditions experienced many years apart are in fact connected, even though these two fields generally exist in their own separate silos. Cardiometabolic disorders of pregnancy, such as pre-eclampsia and gestational diabetes are risks for cardiovascular disease as women age. When you add these risks to preterm delivery and low birth weight, a woman's risk of developing cardiovascular death over a lifetime doubles. At the same time, these cardiometabolic factors, including hypertensive pregnancy, can be associated with life-threatening outcomes during and after childbirth. Clearly, general internists, obstetricians, and cardiologists need to pay much more attention to young women at risk. We are doing better, but we need to do more. At the molecular level, more than two decades of work on the biomarkers of preeclampsia by Dr Ravi Thadhani and Dr Subbian Karumanchi has led to a new FDA-approved diagnostic test to flag those women at greatest risk of life-threatening preeclampsia.

This is an outstanding advance, but our research means little if we don't succeed in translating research into care. Fortunately, black women's poor outcomes in childbirth have been getting some long overdue public attention, in part due to the outstanding journalism of reporters like Linda Villarosa and also to

the terrible first-person stories from celebrities Serena Williams and Beyonce, as well as the tragic death of Olympic sprinter Tori Bowie. Williams said that a day after giving birth, her providers initially dismissed her when she told them that she was having a pulmonary embolism, something she had experienced before. In general, women's healthcare is weakened by a lack of knowledge about sex-specific issues and a lack of respect. Women patients are often not trusted as reliable reporters of their own symptoms, especially black women and other underrepresented minority women. This is an educational challenge for all of us. We need to do better to understand how to effectively teach the next generation of healthcare professionals that quick judgments and implicit bias can undermine the care that they give to patients.

And although we've known this for years, we still are not achieving the behavior changes that we need to see. So, we also need to take a public health approach to the challenge of maternal mortality. Though it has not succeeded in eliminating the mortality gap for black mothers, the state of California has succeeded in keeping its pregnancy-related mortality ratio well below the national ratio with the assistance of the California Maternal Quality Care Collaborative, which was formed in 2006. This partnership between the state Department of Health, Stanford University, and nearly every hospital in the state offers evidence-based toolkits for healthcare providers and hospitals to better prevent, screen for, prepare for, and address maternal risks. Providers around the country should be adopting these best practices that connect academic medicine with public health and healthcare delivery. Of course, even the most advanced healthcare system, healthcare means nothing if someone can't access it.

If we're going to improve health outcomes for women, we need health policies and leadership that support the larger goal of gender equity in our society. Without a question, the Affordable Care Act has dramatically improved access to health insurance and healthcare, and it's been particularly important for women. Before the ACA, many individual plans didn't include maternity coverage, and pregnancies could be treated as pre-existing conditions used to deny women coverage or increase their premiums. However, if you follow the news even slightly today, you know how tenuous these gains are. While our uninsured rate is the lowest it's been in history, we still nearly have 8% of our population uninsured. The lack of expansion of federally covered Medicaid in so many states and the lack of federally mandated paid leave for new mothers are topics that deserve their own talks. And after the Dobbs decision, we now live in a fractured country in terms of health policy. One where women's right to make their own medical decisions is severely limited in many states - the most restrictive here in red - and where doctors are now fearing terminating a pregnancy even to save a woman's life.

So, what can we do to ensure more equitable policies, better clinical care, and more scientifically sound research? Clearly, there's a training aspect. We need to do much more, for example, to educate both scientists and healthcare professionals about the ways that sex differences influence health and disease, not as a single lecture or as an aside, but as a central and integrated component of undergraduate, graduate, and research training. We also need to recognize that who you are influences what you see, and that inclusiveness breeds excellence since a variety of perspectives is so essential to progress and excellence in all fields. We need more women and minorities in position of leadership, in medicine, science, in biotechnology, in the pharmaceutical industry, and in policy and politics. We also need to recognize the ways that the culture of academic medicine and science are hard on women. We are doing better with regard to the percentage of women in medical school and in academic medicine, but they continue to be scarce in scientific leadership, and we have to do better.

One reason is the fact that women in academic medicine and biomedical science encounter bias on all sides. In 2021, we published a paper that demonstrated that journal peer reviewers in the medical sciences are biased against studies focused on women. Now, of course, these studies are more likely to be conducted by women scientists. Even though the reviewers in this study found that studies focused on women were more likely to contribute to medical science, they were nonetheless twice as likely to recommend for publication the same research conducted in men. Unfortunately, publication bias is far from the only insult experienced by women in STEM fields. There's the gender gap in pay and promotions, and there's sexual harassment. In 2018, a committee of the National Academies of Science, Engineering and Medicine published the first evidence-based report on sexual harassment in women in academic science, engineering and medicine. And we found that the academic workplaces are second only to the military in rates of sexual harassment, with women of color experiencing the most harassment.

This is shocking only if you consider it hastily. Although we're improving, these are environments where men outnumber women, especially in leadership, where cultures characterized by disrespect and a lack of civility can develop, creating the conditions where sexual harassment, which includes gender harassment, is more likely to occur. Frankly, all of us in higher ed are working so hard to bring young women into science, engineering and medicine. It's beyond discouraging to think that they are being harassed out of those fields. The National Academies is leading important work in this area as a follow-up to that report. So, where do we go from here? First, I wanna say optimism is in order. We should take heart from the fact that there's a growing understanding that women's health and the study of sex and gender merits much more attention. For example, helping us set a new course is the just released Women's Health Innovation Opportunity Map, sponsored by the Gates Foundation and the NIH office for Research on Women's Health.

It offers 50 ways to improve women's health globally, including improving our data collection and disease modeling. Another promising development, in addition to the centers and labs focused on sex and gender that are represented at this conference, and that you'll hear from today, Rockefeller University has now launched a new center for research on women's health with the support of its vice chair, Marlene Hess, that will explore how sex and gender influence biological processes. Now, given the 26 scientists affiliated with the Rockefeller who've won Nobel Prizes over the years, I have high hopes that the science that emerges will be outstanding. Rockefeller scientists have already led the way in discovering the biology that contributed to the higher death rates observed in men early in the COVID pandemic. The fact that this meeting is devoted to the topic is a major step forward. Second, we need to improve the science that we do and make use of the incredible tools in our hands to move away from the mainly disease-based model of women's health, and to begin understanding the underlying biologic mechanisms that protect women or make them vulnerable.

Third, we need an ecosystem-wide approach to women's health. This includes academic institutions, which are both a producer and an effector arm of science, producing the scientists who serve on study sections, who then decide who gets grants and how the science is performed. Those our institutions need to understand that this is a weak spot and that they have a role in promoting the fact that sex is a critical variable in research. As mentioned earlier, we also need to incorporate this concept into medical education and research training at all levels. So, what else do we need? We need private philanthropy, large and small, to incorporate sex and gender in their major initiatives. We need academic journals to promote a sea change in the way that we do preclinical and clinical research by requiring manuscript



data to be disaggregated by sex. We need the biopharmaceutical industry and device makers to embrace the principles we discussed earlier and make sex an early consideration in research and development.

We need the venture capital industry to wake up to the fact that women are not a niche market, but rather the majority of the population and to start investing in start-ups focused on women's health and run by women. We need to find common ground in this divided country and to determine how and where women's health is being advanced successfully and then replicate these models. We need to keep the health of women at the center of our understanding and addressing the grand challenges of our time, such as climate change. And we need policymakers to ensure that women's health research remains a national priority and to fund it accordingly and hold funding agencies to task. And finally, we need the National Academies to lead the way in setting out a bold and evidence-based agenda, as they so often have in the past, and as we just heard Victor's brilliant talk this morning, as they will do in the future. So, there's a world of opportunity in front of all of us if we focus on improving women's health, to improve the health of everyone, and by extension, to make this a better, more equitable, prosperous, and healthy world.

And again, I'm so delighted to kick off this symposium and I can't wait to hear from my colleagues. Thank you. (AUDIENCE APPLAUSE)